REMARKS

Entry of the foregoing, and further and favorable reconsideration of the subject application pursuant to and consistent with 37 CFR 1.115 are respectfully requested.

By the present Amendment, claims 83-104 have been deleted without prejudice to or disclaimer of the subject matter contained therein. New claims 143-162 have been added. These claims are directed to the same subject matter as original claims 1-12, and similarly derive support from throughout the specification and claims as originally filed. As no Restriction Requirement was issued in connection with the original claims, addition of these claims at the present stage of prosecution is believed to be proper. No new matter has been added by the present Amendment.

Election/Restriction

Applicants hereby renew their traversal of the Restriction Requirement in this case, for the reasons set forth in Applicants' previous response. Applicants further explicitly reserve their right to file divisional applications containing the claims withdrawn and/or deleted from the present application.

Claim Rejections - 35 USC §112

Claims 83-104 are rejected under 35 USC §112, first paragraph, as purportedly lacking written description support in the specification as originally filed. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

Applicants maintain that claims 83-104, and indeed all of the claims that have been pending in the present application, are fully supported by the original specification.

Nevertheless, without conceding to the Examiner's arguments, but solely in an effort to expedite prosecution, claims 13-142 have been deleted, thus rendering this rejection moot.

New claims 143-162 have been added. New claim 143 corresponds, by and large, to original claim 1. However, as will be appreciated by the Examiner, the wording of this claim has been made clearer and more concise. New claim 143 further characterizes the substance that impairs cellular peptide processing for MHC presentation in that tumor cells treated with this substance are subject to specific lysis by CTL elicited by the TAP-deficient variant of said tumor cell which has been transfected with the stimulatory molecule B7-1. For support of this claim, reference is made to page 5, lines 17 to 31, page 7, lines 8 to 12, Figure 2 and Example 2 of the present application.

According to page 7, lines 8 to 12, that a substance induces expression of antigens or epitopes associated with impaired cellular peptide processing, i.e. that a substance impairs cellular peptide processing, may be determined by recognition by effector cells directed against the antigens. These effector cells are T cells elicited by a TAP-deficient tumor cell which has been transfected with the stimulatory molecule B7-1 (see page 5, lines 17 to 31). This is shown for RMA tumor cells in Figure 2 and Example 2. Figure 2 demonstrates that the TAP-deficient tumor cell RMA-S is subject to specific lysis of (i.e. is recognized by) RMA-S.B7-1 elicited CTL, whereas the TAP-2 transfectant variant RMA-S.TAP-2 is only subject to unspecific lysis.

New claims 144 and 145 correspond to original claim 2, whereas new claims 146 and 147 correspond to original claim 3.

New claim 148 pertains to an in vitro process for identifying cells which are capable of activating CD8+ T-lymphocytes that selectively recognize cells showing impaired cellular peptide processing for MHC presentation. This method corresponds to the treatment of cells

to express antigens or epitopes associated with impaired cellular peptide processing described on page 9, line 25 to page 11, line 4 of the present application. The cells to be provided by the method are defined as cells which are capable of activating CD8+ T lymphocytes that selectively recognize cells showing impaired cellular peptide processing for MHC presentation, as described at page 12, lines 1 to 12 of the specification.

New claim 149 further defines the substance to be used in the method of claim 148, and reference is made to the discussion with respect to new claim 144 in this regard. New dependent claims 151 to 154 correspond to new claims 144 to 147, respectively, but now refer back to the method of claim 148.

The subject-matter of new claims 155-156 corresponds to original claim 7.

New claim 157 relates to a composition comprising immunological effector cells, identified by an in vitro process, that selectively recognize cells showing impaired cellular peptide processing for MHC presentation. This process is originally disclosed on page 12, line 14 to line 27 and page 14, line 14 to line 17 of the specification.

New claims 159-160 are composition claims; the composition comprises the cells identified according to the method of claim 148. Support for these claims may be found, for example, in original claim 12 alternative b), and at page 12, lines 1 to 23 of the specification as originally filed.

Claim Rejections - 35 USC §102

Claims 83-85, 87, 88, 90, and 91 are rejected under 35 USC §102(b) as purportedly anticipated by Wölfel et al. (*Eur. J. Immunol.,* 24:759-764, 1994). This rejection, to the extent that it applies to new claims 143-162, is respectfully traversed.

In order to anticipate a claim under 35 USC §102(b), a prior art reference must disclose every element of the claimed invention. *See* MPEP 2131 *et seq.* At page 7 of the Official Action, the Examiner asserts that Wölfel et al. "disclose a method of stimulating T-lymphocytes by contacting said T-lymphocytes with TAP deficient cell lines expressing HLA-A2 molecules which are expressed on blood cells from melanoma patients."

However, Wölfel et al describes T-cells capable of recognizing TAP deficient tumor cells that have been loaded with exogenous peptides. In contrast, the presently claimed invention does not include any exogenous peptides, epitopes, or antigens. Consequently, Wölfel et al does not disclose all of the limitations of the present claims, as required by 35 USC 102(b).

Claims 83-86, 90, 96, 97 and 99 are rejected under 35 USC 102(b) as purportedly anticipated by Zhou et al. (*Scand. J. Immunol.* 42:66-75, 1995). This rejection, to the extent that it applies to new claims 143-162, is respectfully traversed.

At page 6 of the Official Action, the Examiner asserts that Zhou et al. "disclose a method of stimulating T-lymphocytes by contacting T-lymphocytes with TAP deficient T2K Sendai virus cells. Zhou et al. further disclose their methods wherein cells are treated with agents that inhibit cellular peptide processing, for example, BFA."

Zhou et al describes recognition of a TAP independent epitope recognized equally well on TAP-intact and TAP-deficient cells. Consequently, Zhou et al uses an inhibitor only as additional proof of the fact that the epitope is TAP-independent. In contrast, in the presently claimed process epitopes are recognized better on cells with deficiencies in antigen processing or presentation. The use of inhibitors of antigen processing or presentation increases recognition, which is not the case in the process disclosed by Zhou et al. Consequently, because Zhou et al. do not disclose every limitation of the presently claimed invention, as required by 35 USC 102(b), withdrawal of this rejection is respectfully requested.

Claims 83-86, 90, 96, 97, and 99 are rejected under 35 USC 102(b) as purportedly anticipated by Liu et al. (*J. Cell. Immunol.* 154: 3147-3155, 1995). This rejection, to the extent that it applies to new claims 143-162, is respectfully traversed.

At page 8 of the Official Action, the Examiner argues that Liu et al. "Disclose a method of stimulating T-lymphocytes with TAP deficient T2K Sendai virus cells. Liu et al. further disclose their methods wherein the cells are treated with agents that inhibit cellular peptide processing, for example, BFA."

Liu et al describes further research relating to the epitope described by Zhou et al. (above). The major difference between these two publications is that Liu et al describes the use of heat-inactivated epitopes. As described therein, heat inactivation does not influence the TAP-dependence of this epitope. No additional argumentation should be needed then what has already been made in no 4 above.

Conclusion

From the foregoing, further and favorable reconsideration in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

In the event that there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Malcolm K. McGowan, Ph.D.
Registration No. 39,300

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620
Date: September 30, 2002